# General

## Guideline Title

IWGDF guidance on the diagnosis, prognosis and management of peripheral artery disease in patients with foot ulcers in diabetes.

## Bibliographic Source(s)

Hinchliffe RJ, Brownrigg JR, Apelqvist J, Boyko EJ, Fitridge R, Mills JL, Reekers J, Shearman CP, Zierler RE, Schaper NC, International Working Group on the Diabetic Foot. IWGDF guidance on the diagnosis, prognosis and management of peripheral artery disease in patients with foot ulcers in diabetes. Diabetes Metab Res Rev. 2016 Jan;32(Suppl 1):37-44. [38 references] PubMed

## Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

# Recommendations

## Major Recommendations

Note from the National Guideline Clearinghouse (NGC) and the International Working Group on the Diabetic Foot (IWGDF): For the 2015 IWGDF Guidance documents, the IWGDF invited five working groups of international experts to produce guidance on the prevention and management of foot problems in diabetes. Major recommendations provided in the *IWGDF guidance on the diagnosis, prognosis and management of peripheral artery disease in patients with foot ulcers in diabetes* are presented below. See also the NGC summaries of IWGDF guidance on the following related topics:

Prevention of foot ulcers in at-risk patients with diabetes
Footwear and offloading to prevent and heal foot ulcers in diabetes
Diagnosis and management of foot infections in persons with diabetes
Interventions to enhance healing of chronic ulcers of the foot in diabetes

Definitions for the quality of the evidence (High, Moderate, Low, Very Low) and strength of recommendations (Strong, Weak) are provided at the end of the "Major Recommendations" field.

<u>Diagnosis</u>

Which symptoms and signs (clinical examination) should clinicians examine for in a patient with diabetes

in order to identify or exclude peripheral artery disease (PAD)?

> Examine a patient with diabetes annually for the presence of peripheral PAD; this should include, at a minimum, taking a history and palpating foot pulses. (Grading of Recommendations Assessment, Development and Evaluation [GRADE] recommendation: Strong; quality of evidence: Low)
> Evaluate a patient with diabetes and a foot ulcer for the presence of PAD. Determine, as part of this examination, ankle or pedal Doppler arterial wave forms; measure both ankle systolic pressure and systolic ankle brachial index (ABI). (Strong; Low)

Which 'bedside' diagnostic procedure, alone or in combination, has the best performance in diagnosing or excluding PAD in an asymptomatic person with diabetes?

> The guideline authors recommend the use of bedside non-invasive tests to exclude PAD. No single modality has been shown to be optimal. Measuring ABI (with <0.9 considered abnormal) is useful for the detection of PAD. Tests that largely exclude PAD are the presence of ABI 0.9–1.3, toe brachial index ≥0.75 and the presence of triphasic pedal Doppler arterial waveforms. (Strong; Low)

Prognosis

In patients with diabetes and a foot ulcer, which symptoms, signs or bedside tests of PAD or reduced perfusion, and at what level of abnormality, will predict ulcer healing?

> In patients with a foot ulcer in diabetes and PAD, no specific symptoms or signs of PAD reliably predict healing of the ulcer. However, one of the following simple bedside tests should be used to inform the patient and healthcare professional about the healing potential of the ulcer. Any of the following findings increases the pre-test probability of healing by at least 25%: a skin perfusion pressure ≥40 mmHg, a toe pressure ≥30 mmHg or a transcutaneous oxygen pressure (TcPO$_2$) ≥25 mmHg. (Strong; Moderate)
> Consider urgent vascular imaging and revascularization in a patient with a toe pressure <30 mmHg or a TcPO$_2$ <25 mmHg. (Strong; Low)
> Consider vascular imaging and revascularization in all patients with a foot ulcer in diabetes and PAD, irrespective of the results of bedside tests, when the ulcer does not improve within 6 weeks despite optimal management. (Strong; Low)
> Diabetic microangiopathy should not be assumed to be the cause of poor wound healing in patients with a foot ulcer. (Strong; Low)

Which symptoms, signs or bedside tests of PAD, and at what level of abnormality, help predict the risk of future major amputation in patients with diabetes and a foot ulcer?

> In patients with either an ankle pressure <50 mmHg or ABI <0.5, consider urgent vascular imaging and revascularization. (Strong; Moderate)

Treatment

When considering a revascularization, which imaging modalities should be used to obtain anatomical information?

> Color duplex ultrasound, computed tomography angiography, magnetic resonance angiography or intra-arterial digital subtraction angiography can each be used to obtain anatomical information when revascularization is being considered. The entire lower extremity arterial circulation should be evaluated, with detailed visualization of below-the-knee and pedal arteries, in an anteroposterior and lateral plane. (Strong; Low)

What are the aims, outcomes and complications of endovascular therapy and open vascular surgery in people with a foot ulcer in diabetes and PAD?

> The aim of revascularization is to restore direct flow to at least one of the foot arteries, preferably the artery that supplies the anatomical region of the wound. Achieving a minimum skin perfusion

pressure ≥40 mmHg, a toe pressure ≥30 mmHg or a TcPO$_2$ ≥25 mmHg will increase the likelihood of healing. (Strong; Low)

A center treating patients with a foot ulcer in diabetes should have the expertise in and rapid access to facilities necessary to diagnose and treat PAD; both endovascular techniques and bypass surgery should be available. (Strong; Low)

There is inadequate evidence to establish which revascularization technique is superior, and decisions should be made on a number of individual factors, such as morphological distribution of PAD, availability of autogenous vein, patient co-morbidities and local expertise. (Strong; Low)

After a revascularization procedure for a foot ulcer in diabetes, the patient should be treated by a multidisciplinary team as part of a comprehensive care plan. (Strong; Low)

Patients with signs of PAD and a foot infection are at particularly high risk for major limb amputation and require urgent treatment. (Strong; Moderate)

Are there any patients with foot ulcers in diabetes and PAD in whom revascularization interventions should not be performed?

Avoid revascularization in patients in whom, from the patient perspective, the risk–benefit ratio for the probability of success is unfavorable. (Strong; Low)

Is risk reduction for future cardiovascular events feasible in patients with diabetes and an ischemic foot ulcer?

All patients with diabetes and an ischemic foot ulcer should receive aggressive cardiovascular risk management including support for cessation of smoking, treatment of hypertension, control of glycemia and prescription of a statin as well as low-dose aspirin or clopidogrel. (Strong; Low)

<u>Definitions</u>

Recommendations in this guidance were formulated based on the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system for grading evidence when writing a clinical guideline. The authors assessed the quality of evidence on the risk of bias of included studies, effect sizes, and expert opinion, and rated the quality of evidence as 'high,' 'moderate' or 'low.' They assessed the strength of each recommendation as 'strong' or 'weak,' based on the quality of evidence, balance between benefits and harm, patient values and preferences, and costs (resource utilization). The rationale behind each recommendation is described in the original guideline document. See the GRADE Web site [        ] for more information.

# Clinical Algorithm(s)

None provided

# Scope

## Disease/Condition(s)

Diabetic foot ulcers

## Other Disease/Condition(s) Addressed

Peripheral artery disease (PAD)

## Guideline Category

Diagnosis

Evaluation

Management

Risk Assessment

Treatment

# Clinical Specialty

Cardiology

Endocrinology

Family Practice

Internal Medicine

Podiatry

# Intended Users

Advanced Practice Nurses

Nurses

Physician Assistants

Physicians

Podiatrists

# Guideline Objective(s)

To provide recommendations for the diagnosis, prognosis and management of peripheral artery disease (PAD) in patients with foot ulcers in diabetes

# Target Population

Patients with diabetic foot ulcers who have suspected or confirmed peripheral artery disease (PAD)

# Interventions and Practices Considered

Diagnosis/Evaluation/Risk Assessment

Patient history
Palpation of foot pulses
Ankle or pedal Doppler arterial wave forms
Ankle systolic pressure and systolic ankle brachial index (ABI)
Toe pressure
Skin perfusion pressure
Transcutaneous oxygen pressure (TcPO$_2$)
Vascular imaging of lower extremities
    Colour duplex ultrasound

Computed tomography angiography

Magnetic resonance angiography

Intra-arterial digital subtraction angiography

<u>Treatment/Management</u>

Revascularization (angioplasty or bypass surgery)

Treatment by a multidisciplinary team

Aggressive cardiovascular risk management including support for cessation of smoking, treatment of hypertension, control of glycemia and prescription of a statin as well as low-dose aspirin or clopidogrel

# Major Outcomes Considered

- Accuracy and predictive value of tests for diagnosing peripheral artery disease (PAD) and for predicting ulcer healing and amputation risk (sensitivity/specificity, positive/negative likelihood ratios)
- Ulcer healing
- Major amputation
- Limb salvage
- Complications of revascularization
- Morbidity
- Mortality

# Methodology

## Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

## Description of Methods Used to Collect/Select the Evidence

This guidance document is based on three systematic reviews (see the "Availability of Companion Documents" field) on diagnosis, prognosis and treatment (endovascular or bypass) of peripheral artery disease (PAD) in a patient with diabetes and a foot ulcer.

<u>Effectiveness of Bedside Investigations to Diagnose Peripheral Artery Disease among People with Diabetes Mellitus: a Systematic Review</u>

Data Search

A systematic search of the literature was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses guidance. The MEDLINE and EMBASE databases were searched for articles in English language pertaining to the diagnosis of PAD among patients with diabetes from 1980 to June 2014. The results of the search undertaken for a previous systematic review from the International Working Group on the Diabetic Foot (IWGDF) on the effectiveness of revascularization for patients with a diabetic foot ulcer were updated (search version 1, online Appendix A of the systematic review). In addition, a further search (search version 2, online Appendix B of the systematic review) was performed. The abstracts of identified studies were combined and evaluated for inclusion independently by two reviewers, with conflicts adjudicated by a third reviewer. At a later stage, full-text manuscripts of the selected studies were evaluated by two reviewers.

Criteria for Inclusion/Exclusion

Studies evaluating ulcerated and non-ulcerated patients were included to establish the potential effect of ulceration on the performance of diagnostic tests. Diagnostic tests were considered as any specific evaluation that sought to identify the presence of PAD. Serum markers that may be an expression of PAD were included.

Studies eligible for inclusion included those evaluating an index test for PAD against a reference test. Tests considered as an appropriate reference test included digital subtraction angiography (DSA), computed tomography angiography (CTA), magnetic resonance angiography (MRA) and color Doppler ultrasonography (CDUS). Studies comparing two reference tests, defined by the criteria discussed earlier, were excluded. Also excluded were studies involving purely patients with PAD; in studies lacking a non-diseased control group, calculation of sensitivity and/or specificity values was not possible. Only studies reporting separately on ≥10 patients with diabetes were considered, where studies reported on mixed cohorts of patients with and without diabetes; those with a proportion of patients with diabetes <80% were excluded. Studies that reported data in a fashion that did not permit the calculation of sensitivity and/or specificity values, and therefore likelihood ratios, were also excluded.

Performance of Prognostic Markers in the Prediction of Wound Healing or Amputation among Patients with Foot Ulcers in Diabetes: a Systematic Review

Data Search

A systematic search was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses guidance. The MEDLINE and EMBASE databases were searched for English articles pertaining to the diagnosis of PAD among patients with diabetes from 1980 to June 2014. The results of two separate searches were combined. Firstly, a search undertaken for a previous systematic review from the IWGDF on the effectiveness of revascularization of the ulcerated foot was updated (online Appendix A of the systematic review). In addition, a second search was performed with different search terms (online Appendix B of the systematic review). The abstracts of identified studies were combined and evaluated for inclusion independently by two reviewers with conflicts adjudicated by a third reviewer. At a later stage, full-text manuscripts of the selected studies were evaluated by two reviewers

Criteria for Inclusion/Exclusion

Studies evaluating ulcerated patients only were included; those evaluating the prognosis of the asymptomatic (intact) foot were excluded. Cohort studies involving patients undergoing revascularization were included, providing a risk ratio was reported, which was adjusted for revascularization. Studies eligible for inclusion included those evaluating outcome and those based on an index measure of PAD; the studies evaluating demographic factors and their association/predictive value for outcome were excluded.

Included were studies evaluating investigations of PAD/reduced perfusion and their level of abnormality that would predict healing or major amputation. Investigations considered included clinical examination findings, ankle and toe pressures/indices, Doppler waveform analyses, transcutaneous oxygen pressure (TcPO$_2$), laser Doppler imaging, pole test and objective measures of skin temperature. Gold standard tests used to diagnose PAD included magnetic resonance angiography, computed tomographic angiography and digital subtraction angiography and were considered if reported with a cut-off or threshold to predict outcome. Studies that excluded patients with PAD or those with insufficient information on the revascularization status of the cohort during follow-up were excluded. Only studies reporting separately on ≥30 patients with diabetic foot ulceration were considered. Where studies reported on mixed cohorts of patients with and without diabetes; those with a proportion of patients with diabetes of <80% were excluded. Studies that reported data in a fashion that did not permit the calculation of sensitivity and specificity values, and therefore likelihood ratios, were excluded. Also excluded were studies with unspecified or <6-month duration of follow-up.

Effectiveness of Revascularization of the Ulcerated Foot in Patients with Diabetes and Peripheral Artery Disease: a Systematic Review

The MEDLINE and EMBASE databases were searched for articles related to therapies to revascularize the ulcerated foot in patients with diabetes and PAD published from January 1980 to June 2014 (online Appendix S1 of the systematic review). Because of the changing nature of interventions for PAD and improving technology, studies before 1980 were excluded. PAD was defined for the purpose of this systematic review as any flow limiting atherosclerotic lesion of the arteries below the inguinal ligament. All patients included had to have objective evidence of PAD (e.g., angiography or magnetic resonance angiography). Only studies in the English language were included.

The reviewers only selected studies in which >80% of patients had evidence of tissue loss (defined as any lesion of the skin breaching the epithelium or ulceration or gangrene). The diagnosis of diabetes was made according to the individual publication. The reviewers included studies of more than 40 patients where >80% of the population had diabetes or when the results of at least 30 patients with diabetes were reported separately. Studies solely reporting interventions on aortic and iliac arterial disease were excluded because the treatment of supra-inguinal disease in people with diabetes does not differ markedly from that in non-diabetic individuals. Also excluded were studies that had only data on quality of life, on costs and on diagnosis and prognosis of PAD; that were only concerned with medical or topical therapy or on improvement of oxygen delivery; and that compared one form of revascularization technology with another (e.g., various atherectomy devices). Only studies reporting ulcer healing, limb salvage, major amputation or survival as the primary outcome measures were included in the review. Early morbidity or mortality was considered within 30 days or within the first hospital admission. A major complication was defined as any that resulted in a systemic disturbance of the patient or prolonged hospitalization (or as defined by the reporting study).

Patient demographics that were assessed included age, sex, ethnicity and co-morbidities (cardiovascular, renal and cerebrovascular). Reviewers extracted the specifics of the foot lesions where possible, such as site on the foot, depth, presence of infection and stratified when possible according to any previously reported and validated diabetic foot ulcer scoring system. The anatomical distribution of PAD was extracted according to the site of the disease; standard reporting systems were included where possible (e.g., the Trans-Atlantic Inter-Society Consensus Document on Management of Peripheral Artery Disease or Bollinger systems). Objective assessment of perfusion was reported when possible, which included ankle brachial pressure index, toe pressure and transcutaneous oxygen tension. No distinction was made among various endovascular techniques (e.g., angioplasty, stenting, subintimal angioplasty and atherectomy), all being referred to as 'endovascular therapy' or various bypass techniques (e.g., *in situ versus* reversed venous bypass).

The systematic search was performed according to Preferred Reporting Items for Systematic Reviews and Meta-analyses guidelines. Two reviewers assessed studies for inclusion based on titles; two reviewers then excluded studies based on review of the abstract.

## Number of Source Documents

Effectiveness of Bedside Investigations to Diagnose Peripheral Artery Disease among People with Diabetes Mellitus: a Systematic Review

Out of the 6629 studies, a total of ten observational studies reporting data from 2585 patients with diabetes met the study criteria and were included in the qualitative data synthesis (see Table 1 in the systematic review). A flow diagram depicting the overall search results is shown in Figure 1 in the systematic review (see the "Availability of Companion Documents" field).

Performance of Prognostic Markers in the Prediction of Wound Healing or Amputation among Patients with Foot Ulcers in Diabetes: a Systematic Review

From 9476 titles and abstracts, 156 articles were selected for full-text review (see Figure 1 in the systematic review [see the "Availability of Companion Documents" field]). Of these, a total of 11 studies reporting on 5890 patients met the inclusion criteria and were included in the qualitative data synthesis (see online Table 1, Appendix of the online data supplement).

<u>Effectiveness of Revascularization of the Ulcerated Foot in Patients with Diabetes and Peripheral Artery Disease: a Systematic Review</u>

After the identification and screening phase, 958 articles were assessed for eligibility; 57 articles were finally selected for full-text review (see Figure 1 in the systematic review [see the "Availability of Companion Documents" field]). These articles described revascularization of the ulcerated foot in 9029 patients with diabetes and peripheral artery disease (PAD) (see online Table 1). There were no randomized controlled trials (RCTs), but there were four nonrandomized studies with an intervention and control group.

## Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

## Rating Scheme for the Strength of the Evidence

Recommendations in the guidance were formulated based on the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system for grading evidence when writing a clinical guideline. The authors assessed the quality of evidence on the risk of bias of included studies, effect sizes, and expert opinion, and rated the quality of evidence as 'high', 'moderate' or 'low'. See the GRADE Web site [            ] for more information.

## Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

## Description of the Methods Used to Analyze the Evidence

<u>Effectiveness of Bedside Investigations to Diagnose Peripheral Artery Disease among People with Diabetes Mellitus: a Systematic Review</u>

Data Extraction and Quality Assessment

Data were extracted by one reviewer and independently verified by another reviewer. Methodological quality of included studies was assessed independently by the same two reviewers against parameters included in the Quality Assessment of Diagnostic Accuracy Studies (QUADAS) tool, a consensus quality assessment tool designed specifically for diagnostic accuracy studies. Given the heterogeneity of populations studied in observational reports, the measures of test performance were reported separately where possible. For example, if a single study reported separate analyses on a cohort of patients with and without neuropathy, those separate groups are reflected in the evidence table. When not reported in the article, sensitivity and specificity were calculated from raw data, where available, as well as the positive likelihood ratio (PLR) and the negative likelihood ratio (NLR).

The PLR and the NLR were the primary endpoints chosen for this systematic review. A PLR $\geq 10$ and an NLR $\leq 0.1$ were considered markers of good test performance. Given the substantial heterogeneity in both the populations studied and the range of index/reference tests evaluated, a meta-analysis was not performed. The median and range of summary statistics, including estimates of test performance, are presented, stratified by index test and population studied.

<u>Performance of Prognostic Markers in the Prediction of Wound Healing or Amputation among Patients with Foot Ulcers in Diabetes: a Systematic Review</u>

Data Extraction and Quality Assessment

Data were extracted by one observer and independently verified by another reviewer. Methodological quality of included studies was assessed independently by the same two reviewers against parameters included in the Quality in Prognosis Studies (QUIPS) tool. There is no consensus as to deriving an overall score for quality from the QUIPS tool; studies were rated as low quality (0), in which case they were excluded, acceptable (+) or high quality (++). Overall ratings were based on the number of assessment criteria in QUIPS that each study met. If the majority of criteria were met with little or no risk of bias, a '++' rating was given; if most criteria were met but some flaws in the study carried an associated risk of bias, then a '+' rating was allocated. Studies in which most criteria were not met, with significant flaws in key aspects of the study design, including accounting for confounding and completeness of follow-up, were rated as '0' and excluded (see Figure 1 in the systematic review [see the "Availability of Companion Documents" field]). Given the heterogeneity of populations studied in observational reports, the predictive values of test performance were reported separately where possible. For example, if a single study reported separate analyses on a cohort of patients with and without neuropathy, those separate groups are reflected in the evidence table. When not reported in the article, sensitivity, specificity and risk ratios (RR) were calculated from raw data, in addition to the PLR and NLR.

The PLR and NLR were the primary endpoints chosen for this systematic review. Likelihood ratios provide the most meaningful comparator for clinical decision-making. A PLR is the number of times more likely a particular test result is present in a person with a particular outcome compared with the likelihood of this result in a person without the outcome. In contrast, a NLR is the likelihood of a negative test in an individual without the outcome compared with a person who experiences the outcome. A PLR $\geq 10$ and a NLR $\leq 0.1$ were considered markers of good test performance. Where information on mortality was provided, the healing and amputation status of an individual at death defined their outcome. Given substantial heterogeneity in both the populations studied and the range of index PAD measures evaluated, a meta-analysis was not performed. The median and range of summary statistics, including estimates of predictive performance, are presented, stratified by index test and population studied.

Effectiveness of Revascularization of the Ulcerated Foot in Patients with Diabetes and Peripheral Artery Disease: a Systematic Review

The systematic search was performed according to Preferred Reporting Items for Systematic Reviews and Meta-analyses guidelines. Two reviewers assessed studies for inclusion based on titles; two reviewers then excluded studies based on review of the abstract and reviewed the full text of selected articles for quality rating; the data for the evidence table were extracted by one author. Studies were assessed for methodological robustness, using the Scottish Intercollegiate Guidelines Network (SIGN) instrument as follows: level 1 includes meta-analyses and randomized controlled trials (RCTs), and level 2 includes studies with case-control, cohort, controlled before-after or interrupted time series design. Studies were rated as ++ (high quality with low risk of bias), + (well conducted with low risk of bias) and − (low quality with higher risk of bias), according to the SIGN methodological quality score. Level 3 studies, that is, those without a control group, such as case series, were not rated. Pooling of data (and therefore weighting of studies) was not possible because of study heterogeneity and the generally low quality of evidence. When several studies reported on a specific item, the data of these separate studies were summarized as interquartile ranges (IQRs) and median. It should be noted that these figures are not weighted means.

# Methods Used to Formulate the Recommendations

Expert Consensus

# Description of Methods Used to Formulate the Recommendations

Following the systematic review, the experts in the working group formulated recommendations based on

the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system for grading evidence when writing a clinical guideline. The GRADE system allows the experts to provide a rating for each recommendation based on both the strength with which it is recommended and the quality of the evidence underlying it. In this manner the link is made between scientific evidence and recommendations for daily clinical practice (see the "Rating Scheme for the Strength of the Recommendations" field).

## Rating Scheme for the Strength of the Recommendations

Recommendations in the guidance were formulated based on the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system for grading evidence when writing a clinical guideline. The authors assessed the strength of each recommendation as 'strong' or 'weak', based on the quality of evidence, balance between benefits and harm, patient values and preferences, and costs (resource utilization). See the GRADE Web site _____ for more information.

## Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

## Method of Guideline Validation

Internal Peer Review

## Description of Method of Guideline Validation

Consensus

The members of the International Working Group on the Diabetic Foot (IWGDF) Editorial Board met in person on a number of occasions to thoroughly review the systematic reviews and the guidance documents, which were then revised by the working group based on this editorial review. When found satisfactory, the Editorial Board sent the guidance document to the IWGDF representatives for comments; the editorial board processed all comments received and made changes where needed in collaboration with the chair of the working group.

# Evidence Supporting the Recommendations

## Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

# Benefits/Harms of Implementing the Guideline Recommendations

## Potential Benefits

- Peripheral artery disease (PAD) is more common in patients with diabetes, and around half of patients with a diabetic foot ulcer have coexisting PAD. Identifying PAD among patients with foot ulceration is important because its presence is associated with worse outcomes, such as a slower (or

lack of) healing of foot ulcers, lower extremity amputations, subsequent cardiovascular events and premature mortality.

- A revascularization procedure can have several aims, such as promotion of wound healing, helping to resolve infection and avoiding or limiting the level of amputation.
- In one follow-up study in patients with a neuro-ischemic foot ulcer, introduction of aggressive cardiovascular risk management (i.e., antiplatelet agent, statin and antihypertensive medication when indicated) reduced 5-year mortality from 58% to 36%.

Refer to the "Rationale" sections in the original guideline document for an assessment of balance of benefits and harms for each recommendation.

## Potential Harms

- Revascularization of the lower limb in patients with diabetes and peripheral artery disease (PAD) can be a particularly high-risk procedure. Patients with a diabetic foot ulcer and PAD have high rates of co-morbidities, such as cardiovascular and renal disease. If there is no possibility of wound healing or when major amputation is inevitable, revascularization should not be considered; an exception is when transtibial amputation is considered and there is no popliteal or femoral pulse; then investigation and vascular intervention should be considered.
- The perioperative mortality rates of revascularization procedures in patients with diabetes and an ischemic foot ulcer are <5% in most studies, but major systemic in-hospital complications have been observed in about 10% of the patients in both open and endovascular series, probably reflecting the poor general health of these patients. The outcomes in patients with diabetes and end-stage renal disease are worse, with a 5% perioperative mortality and 1-year mortality of approximately 40%. However, even in these patients, favorable results can be obtained, but the majority of studies report 1-year limb salvage rates of approximately 70%.

Refer to the "Rationale" sections in the original guideline document for an assessment of balance of benefits and harms for each recommendation.

# Qualifying Statements

## Qualifying Statements

Not stated

# Implementation of the Guideline

## Description of Implementation Strategy

Guidelines will be implemented via the training programs of the International Working Group on the Diabetic Foot (IWGDF) as well as with support of the translation of the guidelines in local languages.

## Implementation Tools

Quick Reference Guides/Physician Guides

> For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

# Institute of Medicine (IOM) National Healthcare Quality Report Categories

## IOM Care Need

Getting Better

Living with Illness

## IOM Domain

Effectiveness

Patient-centeredness

# Identifying Information and Availability

## Bibliographic Source(s)

Hinchliffe RJ, Brownrigg JR, Apelqvist J, Boyko EJ, Fitridge R, Mills JL, Reekers J, Shearman CP, Zierler RE, Schaper NC, International Working Group on the Diabetic Foot. IWGDF guidance on the diagnosis, prognosis and management of peripheral artery disease in patients with foot ulcers in diabetes. Diabetes Metab Res Rev. 2016 Jan;32(Suppl 1):37-44. [38 references] PubMed

## Adaptation

Not applicable: The guideline was not adapted from another source.

## Date Released

2016 Jan

## Guideline Developer(s)

International Working Group on the Diabetic Foot - Nonprofit Organization

## Source(s) of Funding

International Working Group on the Diabetic Foot

## Guideline Committee

International Working Group on the Diabetic Foot

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## Financial Disclosures/Conflicts of Interest

The International Working Group on the Diabetic Foot Guidance is developed by working groups of independent experts. These documents are written without any influence from commercial, political, academic or other interest groups.

## Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

## Guideline Availability

Available from the Diabetes/Metabolism Research and Reviews Web site             .

## Availability of Companion Documents

The following are available:

Hinchliffe RJ, Brownrigg JR, Apelqvist J, Boyko EJ, Fitridge R, Mills JL, Reekers J, Shearman CP, Zierler RE, Schaper NC. Effectiveness of bedside investigations to diagnose peripheral artery disease among people with diabetes mellitus: a systematic review. Diabetes Metab Res Rev. 2016 Jan;32(Suppl 1):119-27. Available from the Diabetes/Metabolism Research and Reviews Web site             .

Hinchliffe RJ, Brownrigg JR, Apelqvist J, Boyko EJ, Fitridge R, Mills JL, Reekers J, Shearman CP, Zierler RE, Schaper NC. Performance of prognostic markers in the prediction of wound healing or amputation among patients with foot ulcers in diabetes: a systematic review. Diabetes Metab Res Rev. 2016 Jan;32(Suppl 1):129-35. Available from the Diabetes/Metabolism Research and Reviews Web site             .

Hinchliffe RJ, Brownrigg JR, Apelqvist J, Boyko EJ, Fitridge R, Mills JL, Reekers J, Shearman CP, Zierler RE, Schaper NC. Effectiveness of revascularization of the ulcerated foot in patients with diabetes and peripheral artery disease: a systematic review. Diabetes Metab Res Rev. 2016 Jan;32(Suppl 1):136-44. Available from the Diabetes/Metabolism Research and Reviews Web site             .

Bakker K, Apvelqvist J, Lipsky BA, Van Netten JJ, Schaper NC, International Working Group on the Diabetic Foot (IWGDF). The 2015 IWGDF guidance documents on prevention and management of foot problems in diabetes: development of an evidence-based global consensus. Diabetes Metab Res Rev. 2016 Jan;32(Suppl 1):2-6. Available from the Diabetes/Metabolism Research and Reviews Web site             .

Schaper NC, Van Netten JJ, Apelqvist J, Lipsky BA, Bakker K, International Working Group on the Diabetic Foot (IWGDF). Prevention and management of foot problems in diabetes: a summary

guidance for daily practice 2015, based on the IWGDF Guidance Documents. Diabetes Metab Res Rev. 2016 Jan;32(Suppl 1):7-15. Available from the Diabetes/Metabolism Research and Reviews Web site ⬚.

## Patient Resources

None available

## NGC Status

This NGC summary was completed by ECRI Institute on November 4, 2016. The information was verified by December 11, 2016.

## Copyright Statement

# Disclaimer

## NGC Disclaimer